

REMARKS

Entry of the foregoing amendments are respectfully requested.

Should the Examiner have any questions concerning the subject application, a telephone call to the undersigned would be appreciated.

Respectfully submitted,

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Attachment t Preliminary Amendment dated March 26, 2001

Marked-up Claims 1-20, 24 and 25

1. (Amended) [Biological] A biological material [for preparing pharmaceutical compositions intended] for treating mammals, comprising:
 - either at least one nucleic acid sequence containing at least one gene of therapeutic interest and elements which ensure the expression of said gene *in vivo* in target cells intended to be genetically modified with said nucleic acid sequence;
 - or at least one target cell which does not naturally produce antibodies and which is genetically modified *in vitro* with at least one nucleic acid sequence above, [characterized in that] said gene of therapeutic interest encodes all or part of an antibody which will be expressed at the surface of said target cell, [and in that] wherein said antibody is capable of binding to a polypeptide which is present at the surface of a cytotoxic effector cell or of a helper T lymphocyte, and which is involved in the process of activation of such a cell.
2. (Amended) [Biological] The biological material according to claim 1, [characterized in that] wherein said nucleic acid sequence is in the form of a naked DNA or RNA sequence.
3. (Amended) [Biological] The biological material according to claim 1, [characterized in that] wherein said nucleic acid sequence is a vector which allows the transfer of said gene of therapeutic interest into said target cells.
4. (Amended) [Biological] The biological material according to claim 3, [characterized in that] wherein said vector is a viral vector.

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5. (Amended) [Biological] The biological material according to claim 4, [characterized in that] wherein said viral vector is an adenoviral or retroviral vector, or a poxvirus, [in particular] optionally derived from the vaccinia virus or from the Modified Virus Ankara (MVA).

6. (Amended) [Biological] The biological material according to claim 3, [characterized in that] wherein said vector [consists of] comprises at least one said nucleic acid sequence complexed with or substance selected from the group consisting of a cationic amphiphile, [in particular a cationic lipid,] a cationic or neutral polymer, a protic polar compound [in particular chosen from propylene glycol, polyethylene glycol, glycerol, ethanol and 1-methyl-L-2-pyrrolidone or their derivatives], and an aprotic polar compound [in particular chosen from dimethyl sulfoxide (DMSO), diethyl sulfoxide, di-n-propyl sulfoxide, dimethylsulfone, sulfolane, dimethylformamide, dimethylacetamide, tetramethylurea and acetonitrile], or their derivatives.

7. (Amended) [Biological] The biological material according to [any one of the preceding claims] claim 1, [characterized in that] when said nucleic acid sequence [contains] comprises a gene encoding the heavy chain of an antibody capable of binding to a polypeptide which is present at the surface of a cytotoxic effector cell or of a helper T lymphocyte, and which is involved in the process of activation of such a cell, fused with a transmembrane polypeptide.

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8. (Amended) [Biological] The biological material according to claim 7, [characterized in that] wherein said nucleic acid sequence [also] further contains a gene encoding the light chain of an antibody capable of binding to a polypeptide which is present at the surface of a cytotoxic effector cell or of a helper T lymphocyte, and which is involved in the process of activation of such a cell.

9. (Amended) [Biological] The biological material according to [either of claims 7 and 8] claim 7, [characterized in that] wherein said transmembrane polypeptide is selected from the group consisting of a glycoprotein, a lipoprotein and a membrane receptor.

10. (Amended) [Biological] The biological material according to claim 9, [characterized in that] wherein said transmembrane polypeptide is selected from the group consisting of the rabies virus glycoprotein, gp160 and CD4.

11. (Amended) [Biological] The biological material according to [any one of the preceding claims] claim 1, [characterized in that] wherein said polypeptide which is present at the surface of a cytotoxic effector cell or of a helper T lymphocyte, and which is involved in the process of activation of such a cell, is a receptor.

12. (Amended) [Biological] The biological material according to claim 11, [characterized in that] wherein said cytotoxic effector cell is selected from the group consisting of macrophages, cytotoxic T lymphocytes (TCLS) and killer cells (NKs) or their derived cells.

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13. (Amended) [Biological] The biological material according to [either of claims 11 and 12] claim 11, [characterized in that] wherein said receptor [is selected from the group consisting of] comprising all or part of the TCR complex[, more particularly TCR- α , TCR- β or CD3, CD8, CD4, CD28, LFA-1, 4-1BB, CD47, CD2, CD9, CD45, CD40, receptors for cytokines, such as IL-7, IL-4, IL-2, IL-15 or GM-CSF, V α 14NKT, NKAR and the Fc receptor].

14. (Amended) [Biological] The biological material according to [any one of the preceding claims] claim 1, [characterized in that] wherein said target cell is a mammalian tumor cell, a mammalian cell infected with a viral pathogenic agent, or a mammalian cell infected with a bacterial pathogenic agent.

15. (Amended) [Biological] The biological material according to claim 1, [characterized in that it consists of] which comprises at least one target cell which does not naturally produce antibodies, in a form which allows their administration to the body of a mammal, and optionally their culturing beforehand, said cell being genetically modified *in vitro* with at least one nucleic acid sequence containing at least one gene encoding all or part of an antibody which is expressed at the surface of said target cell, and [in that] wherein said antibody is capable of binding to a polypeptide which is present at the surface of a cytotoxic effector cell or of a helper T lymphocyte, and which is involved in the process of activation of such a cell.

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16. (Amended) [Biological] The biological material according to claim 15, [characterized in that] wherein said target cells originate from the mammal to be treated.

17. (Amended) [Biological] The biological material according to claim 15, [characterized in that] wherein said target cells originate from a mammal other than the one to be treated and have undergone a treatment making them compatible.

18. (Amended) [Biological] The biological material according to [one of claims 1 to 17] claim 1, [characterized in that it is also] which further comprises at least one DNA sequence which ensures the expression of a compound which is involved in the activation of cytotoxic effector cells or of helper T lymphocytes.

20. (Amended) [Use of] A method for a nucleic acid sequence containing at least one gene of therapeutic interest and elements which ensure the expression of said gene *in vivo* in target cells genetically modified with a said nucleic acid sequence, said gene of therapeutic interest encoding all or part of an antibody which is expressed at the surface of said target cell, and which is capable of binding to a polypeptide which is present at the surface of a cytotoxic effector cell or of a helper T lymphocyte, and which is involved in the process of activation of such a cell, for preparing pharmaceutical compositions intended for treating a mammal by gene transfer.

21. (Amended) Pharmaceutical composition comprising a biological material according to [one of claims 1 to 18] claim 1 advantageously in combination with a pharmaceutically acceptable vehicle.

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23. (Amended) Pharmaceutical composition according to claim [22] 29, characterized in that said compound is a cytokine or a chemokine.

24. (Amended) Mammalian cell which does not naturally produce antibodies, [characterized in that it] which is genetically modified with at least one nucleic acid sequence containing at least one gene of therapeutic interest and elements which ensure the expression of said gene in said cell, said gene of therapeutic interest encoding all or part of an antibody which is expressed at the surface of said genetically modified cell, and [in that] wherein said antibody is capable of binding to a polypeptide which is present at the surface of a cytotoxic effector cell or of a helper T lymphocyte, and which is involved in the process of activation of such a cell.

25. (Amended) Method for preparing a cell according to claim 24, [characterized in that] said method comprising an effective amount of at least one nucleic acid sequence containing at least one gene of therapeutic interest and elements which ensure the expression of said gene in said cell, said gene of therapeutic interest encoding all or part of an antibody which is expressed at the surface of said genetically modified cell, [is introduced] into a mammalian cell which does not naturally produce antibodies, by any suitable means, and [in that] wherein said antibody is capable of binding to a polypeptide which is present at the surface of a cytotoxic effector cell or of a helper T lymphocyte, and which is involved in the process of activation of such a cell, and [then in that, from these

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cells,] selecting those cells which are genetically modified with said nucleic acid sequence
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